UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,953	12/10/1998	OYSTEIN FODSTAD	7885.56USWO	8358

7590 06/15/2004

MERCHANT & GOULD P.C.
P.O. BOX 2903
MINNEAPOLIS, MN 55402

EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/125,953	FODSTAD ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,6-9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,6-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 2, 3, 6-9 and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over SmithKline Beecham Corporation (WO 95/21944; SmithKline) in view of Høifødt et al. (WO 95/24648).

5. Smithkline, page 3, last paragraph, and pages 13-14, disclose method for conducting differential hybridization whereby genes differentially expressed in disease tissue as compared to healthy/normal tissue are identified. At page 3, lines 16-17, discloses employing these methods so to provide methods of diagnosis of diseases. By determining which genes are differentially expressed, and the level at which they are expressed, one also determines the level of mRNA expression. In support of this position attention is directed to page 3, last paragraph, and to page 13, first full paragraph, which teaches that mRNA and/or can is isolated from the biological sample from both healthy and diseased individuals. Also disclosed is the cloning of genes identified through the disclosed processes, e.g., subtractive hybridization. This meets a limitation of claims 6 and 7.

6. SmithKline does not teach immunomagnetically isolating the cells prior such that nearly 100% specific target cells are obtained.

7. Høifødt et al., page 3, discloses using immunomagnetic methods to not only detect but to isolate target cells in an otherwise mixed population of cells. Page 7, line 21, bridging to page 8, line 9, discloses using immunomagnetic separation for the establishment of "a pure population of target cells" such that one can examine genes at the "DNA, RNA and protein level." The aspect of achieving "a pure population of target cells" is considered to meet the limitation that one obtains a "nearly 100% specific target cell [population]."

8. Høifødt et al., page 4, last paragraph, bridging to page 5, teaches that their method of immunomagnetic separation of cells overcomes prior difficulties in being able to readily isolate diseases (e.g., malignant) cells in a heterogeneous mixture of cells. Høifødt et al., also teach explicitly that their method is "very sensitive."

9. Høifødt et al., at pages 21-25 (Table 1) provides an exhaustive listing of antigens and antibodies that can be used to isolate specific cells which in turn can be used or the subject of further investigation.

10. Høifødt et al., page 8, first paragraph, discloses the applicability of the immunomagnetic separation where one would be able to identify new genes associated with tumor cells, where the tumor can be malignant (page 8, line 5) and can be found in bodily fluids (page 8, line 6). This meets a limitation of claims 2 and 3.

11. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have combined the method of Høifødt et al., with that of SmithKline as the ordinary artisan would have been able to isolate target (pathogenic) cells both easily and with a high degree of sensitivity and to then use this enriched population of cells in the subtractive hybridization assay disclosed by Smithkline whereby genes differentially expressed are identified. In view of the explicit teachings of suitable antigens and antibodies provided by Høifødt et al., and the detailed guidance as to how differentially-expressed genes can be isolated from different tissues (SmithKline), the ordinary artisan would have been amply motivated and would have had a most reasonably expectation of success. For the above reasons, and in the absence of convincing evidence to the contrary, claims 2, 3, 6-9, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the prior art of record.

Response to argument

12. Agreement is found where at page 3 of applicant's response of 22 January 2004 it is asserted that it may be difficult to obtain normal and diseased tissue when the cells exist in a mixture. And agreement is reached in that SmithKline does not teach isolation or enrichment of cell populations. However, the rejection is not predicated on the disclosures of SmithKline alone, but rather, over the combined teachings of SmithKline and Høifødt et al. As noted above, Høifødt et al., teach explicitly of enriching pathogenic (malignant) cells that have invaded otherwise normal tissue.

13. At page 3 of the response applicant asserts that the method of SmithKline was well known to have problems, yet in spite of these well known problems, one would not be motivated to do otherwise. This argument has been fully considered and has not been found persuasive for if the method of SmithKline was know to have problems, one of ordinary ski in the art would be motivated to devise a method whereby such problems could be reduced if not eliminated. Accordingly, one of ordinary skill would have been motivated to incorporate the steps of cell enrichment/purification as disclosed by Høifødt et al. and in so doing avoid the very problems that applicant asserts were well known in the art.

14. At page 4 of the response applicant asserts that their method is "[c]ompletely different from the teaching of Høifødt [in that] Applicant's method compares gene expression profiles in tumor cells enriched from different sites/tissues in the same individual."

15. The above argument has been fully considered and has not been found persuasive as applicant is arguing limitations not found in the claims. While the method of claim 12, the only independent claim, requires one to use a first and second tissue sample, either one or both of the

samples could be normal or pathogenic. Further, the claim does not proscribe taking two samples from the same tissue, or that the second sample could be a portion of a first sample.

16. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

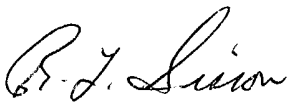
17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

18. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

20. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
12 June 2004